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Metabolomics

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ABSTRACT

A brief review on metabolomics, a new field being explored, which provides information regarding mechanisms of human health and diseases. Metabolomics deals with study of blood metabolites, circulating small molecules likes amino acids, lipids (fats), nucleotides, and carbohydrates involved in metabolism. Research on diseases like diabetes, kidney disease, and heart disease revealed dysfunction at molecular level before the actual clinical symptoms of the disease appear. Scientist have tried gene studying for knowledge of human body and diseases, but there are about 20,000 to 25,000 genes which encodes more than million proteins which further change into functionally modified proteins hence metabolomics comparatively has a decisive edge since there are only 3,000 to 6,000 metabolites of interest currently.

KeyWords

Metabolomics and metabolome.

Abbreviation

HMDB, human metabolome database, NMR, nuclear magnetic resonance, CE, capillary electrophoresis, GC, gas chromatography, MS, mass spectrometry.

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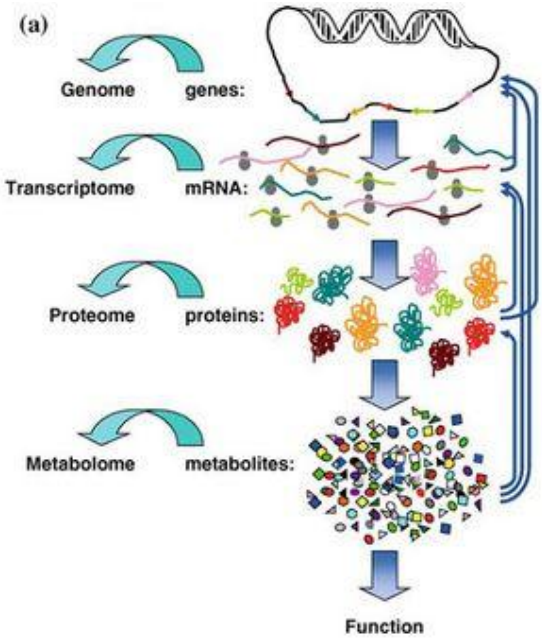
INTRODUCTION

The name metabolomics was first used in late 1990's and first paper mentioning the word metabolome was Systematic Functional Analysis of Yeast Genome by Oliver, S. G., Winson, M. K., Kell, D. B. & Baganz, F. in 1998. Human metabolome project, a first draft of human metabolome in 2007. The human metabolome project is $7.5 million project funded by Genome Canada launched in 2005. The purpose of this project was research in metabolomics for several objectives like improved disease identification, prognosis, monitoring, knowledge about drug metabolism and toxicology, provide linkage between human metabolome and human genome, and developing software tools for metabolomics.

Metabolomics basically deals with metabolic products of human genome. Metabolomics is an advanced approach compared to genomics and proteomics strategies for probing human diseases because of its immediate clinical impact involving rapid and high throughput characterization of small molecule metabolites present in an organism.

Metabolomics is study of metabolome, A metabolome is closely related to genotype of an organism, therefore metabolome is collection of all metabolites in an organism which are end products of gene expression. These metabolites include metabolic intermediates, hormone, other signalling molecules and secondary metabolites found within a biological sample.

Ergo, metabolomics is study of complete collection of metabolites present in cell or tissue for generating a biochemical profile and 'Omics' for small molecule.



This is schematic representation of Omic starting with genomics, transcriptomics, proteomics, and metabolomics.

Metabolomics and metabonomics differ in way of approach where the later is applied to study of human nutrition and reponses to drugs or diseases without identifying individual compounds.

A metabolome consists of chemical compounds from ionic inorganic species to hydrophilic carbohydrates, hydrophobic lipids, volatile alcohols and ketones, amino, non-amino organic acids, and complex natural products. Due to complex nature of metabolomes several different extraction and analysis procedures are used and results are combined to give complete biochemical data on large number of metabolites.

In human genomics, the human genome is fully sequenced and accessible but metabolomics is not well developed as there are 2900 metabolites detectable in human body but all metabolites cannot be found in tissue or biological fluid because they have different metabolic roles.

The human metabolome project has identified and quantified 309 metabolites in cerebrospinal fluid, 1122 metabolites in serum, 458 metabolites in urine and 300 metabolites in other tissue and biological fluids.

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HUMAN METABOLOME DATABASE

The human metabolome database (HMDB) is a freely available electronic database containing information about small molecule metabolites found in human body used for applications in clinical chemistry, metabolomics, and biomarker discovery. The database version is 3.0, contains 40260 metabolites including water soluble and lipid soluble metabolites as well as 5617 protein (DNA) sequences linked to these metabolites. These data fields are linked to KEGG, PubChem, MetaCyc, ChEBI, PDB, Swiss-Prot, and GenBank. The HMDB database supports chemical structure, and relational query searches. Databases like DrugBank, T3DB, SMPDB, FooDB are also part of HMDB. The HMDB database contains 3 kinds of data

1. Chemical data.
2. Clinical data.
3. Molecular biology/biochemistry data.

HMDB is supported by David Wishart, Department of Computer Science and Biological sciences, University of Alberta and The Metabolomics Innovation Center.

STEPS IN METABOLOMICS

1. Biochemical analysis of metabolites.
2. Identification and measurement of metabolites in cell, tissue, and biological fluid.
3. Characterization of endogenous and exogenous factors on metabolite composition and networks.
4. Elucidating the biological process.
5. Using diagnostic, prognostic, therapeutic tool, high through output techniques like NMR, MS, CE for detection of contents.

Results obtained are useful in obtaining knowledge of composition of metabolites, system of metabolic networks, and process that affects metabolism.

ANALYSIS OF METABOLOMICS

1. Sample preparation
2. Seperation of analytes.
3. Detection.
4. Identification and quantification.

SAMPLE PREPARATION

In biological system due to wide variations in ranges of concentrations and secondary metabolites in plants, the composition and quantity of metabolites detected depends a large extent on the sample preparation chosen and the extent of metabolomes detected depends on content of biological sample. More the steps in sample preparation (sequential extractions and concentrations to favour a particular compound) narrower will chemical diversity of compounds finally obtained.

For reproducible measurements, the sample should be homogenous in aspects of environmental conditions like light, temperature, humidity, nutrients, and time of sampling.

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For metabolomics, a fast, reproducible, and unselective extraction method is preferred to avoid chemical modifications.

EXTRACTION METHODS

1. Liquid extraction
2. Solid-phase extraction
3. Solid-phase microextraction
4. Microwave assisted extraction

SEPERATION OF ANALYTES

1. Gas chromatography.
2. Capillary electrophoresis.
3. High performance liquid chromatography (HPLC).
4. Ultra performance liquid chromatography (UPLC).

Gas Chromatography

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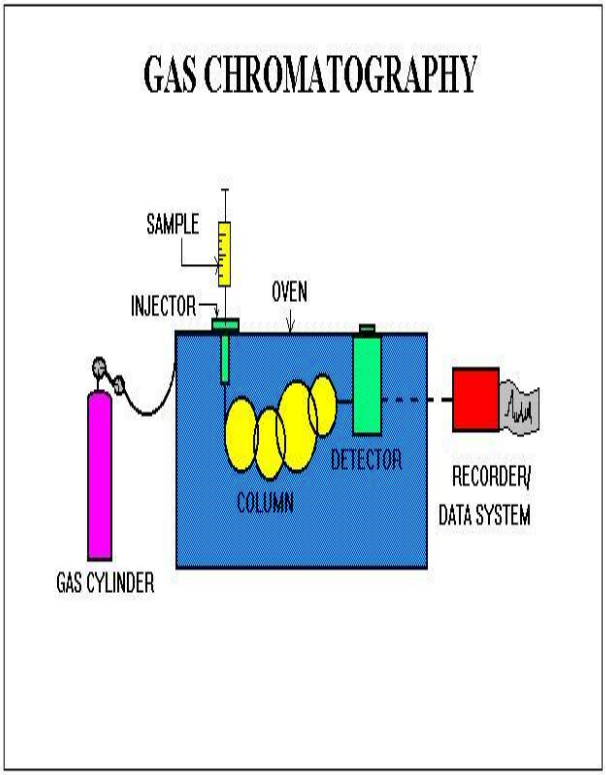
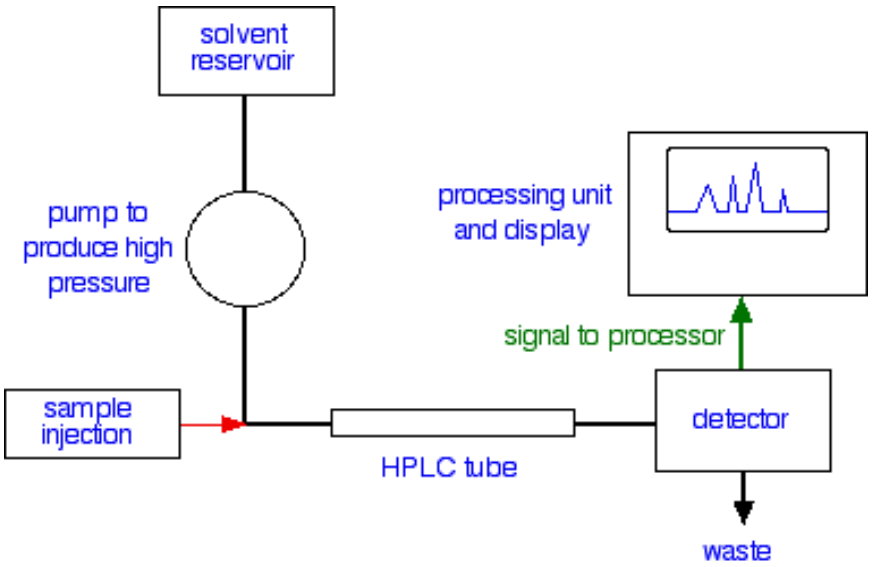


Used in organic chemistry. Provides high chromatographic resolution. Requires chemical derivatization.

HPLC



Used in biochemistry and analytical chemistry, provides lower chromatographic resolution. Capillary electrophoresis Higher separation efficacy than HPLC, provides wide range of metabolites.

DETECTION

Nuclear magnetic resonance (NMR) & Mass spectrometry (MS).

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The relative strengths and weaknesses of nuclear magnetic resonance and mass spectrometry for metabolic profiling[a]

	NMR	MS
Detection limits	Low-micromolar at typical observation frequencies (600 MHz), but nanomolar using cryoprobes	Picomolar with standard techniques, but can be much lower with special techniques
Universality of metabolite detection	If metabolite contains hydrogens it will be detected, assuming the concentration is sufficient or protein binding does not cause marked line broadening	Usually needs a more targeted approach. There can be problems with poor chromatographic separation; with the loss of metabolites in void volumes; with ion suppression (but this is reduced when using UPLC); lack of ionization; ability to run both +ve and −ve ion detection gives extra information
Sample handling	Whole sample analyzed in one measurement	Different LC packings and conditions for different classes of metabolite; usually samples have to be extracted into a suitable solvent; samples have to be aliquoted but some recent studies have avoided the need for chromatography
Amount of sample used	Typically 200–400 μL, but much less for microcoil probes, down to 5–10 μL	Low μL range
Sample recovery	Technique is nondestructive	Technique is destructive but only small amounts used
Analytical reproducibility	Very high	Fair
Sample prepreparation	Minimal: addition of buffer, D_2O and chemical shift reference (not always required)	Can be substantial; often needs different LC columns and protein precipitation
Ease of molecular identification	High, both from databases of authentic material and by self-consistent analysis of 1D and 2D spectra	Difficult, often only the molecular ion is available; this needs extra experiments, such as routine tandem MS; GC-MS is generally better with accurate retention times and comprehensive databases of spectra
Time to collect basic data	5 min for 1D ^1H NMR	10 min for UPLC-MS run
Quantitation	1–5%	5% intraday and interday is now common with or without prior chromatography
Robustness of instruments	High	Low
Molecular dynamics information	Yes, from T1, T2 relaxation time and diffusion coefficient measurements	No
Analysis of tissue samples	Yes, using MAS NMR	No
Availability of databases	Not yet comprehensive but increasing; several are available freely on the web; some commercial products also exist	Comprehensive databases for electron impact MS allow spectral comparisons; For electrospray ionization, as is usual in LC-MS, only mass values can be compared

DATA ANALYSIS AND INTERPRETATION

1. Chemometric approach.

   Principle Component analysis (PCA).

   Soft independent Modelling of Class Analogy (SIMCA).

   Partial Least-Squares (PLS) method by Projection to Latent Structures.

   Orthogonal PLS (OPLS).

2. Target Profiling.

FIELDS OF METABOLOMICS APPLICATION

3. Plant breeding and assessment of crop quality.
4. Food assessment and safety.
5. Toxicity assessment.
6. Nutrition assessment.
7. Medical diagnosis and assessment of disease status

.Pharmaceutical drug development.

8. Yield improvement in crops and fermentation.
9. Biomarker discovery.
10. Technological advances in analytical chemistry.
11. Genotyping.

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12. Environmental adaptations.
13. Gene-function elucidation.
14. Integrated systems biology.

REFERENCE

[1] Moselio Schaechter, (21, May, 2009), American Society for Microbiology, Metabolomics and Metabonomics.

[2] Fathoming Metabolomics, (May-June 2011) Harvard Magazine.

[3] Metabolomics Toolbox, the Human Metabolome Project, Genome Alberta, Canada.

[4] Human Metabolome Database version 3.0.

[5] Josephine, Linke, Yibetal, Overview of Metabolomics, PPT.

[6] Sofia Moco, Raoul J. Bino, Ric C.H. De Vos, Jacques VerVoort, Trends in Analytical Chemistry, Vol 26, No.9 2007, Metabolomics Technologies and metabolite identification.

[7] Soumen Kanti Manna, Laboratory of Metabolism Center for Cancer Research NCI, NJH, An introduction to metabolomics.